

2,2-bis(Bromomethyl)-1,3-propanediol

CAS #3296-90-0

Swiss CD-1 mice, at 0.0, 0.1, 0.2, and 0.4% in feed

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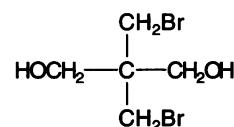
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2,2-bis(Bromomethyl)-1,3-propanediol (BBMP), a widely used flame retardant for a variety of foams, was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol (Treinen et al., *Fundam Appl Toxicol* 13:245-255 [1989]). Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation phase at 0.1, 0.2, and 0.4% in feed. Based on body weights and food consumption, the estimated daily doses were approximately 141, 274, and 589 mg/kg.

One middle dose female and one high dose female died during the study from causes considered unrelated to BBMP exposure. Body weight gain for all treated groups was less than in controls; body weight means were reduced for females at the middle and high doses by 6 to 16%, and for high dose males by less than or equal to 10%.

At the high dose, the number of litters per pair and the number of pups per litter were reduced by 12 and 44%, respectively. Pup body weight, adjusted for litter size, was reduced by 5 and 8% at the middle and high doses, respectively. Additionally, the cumulative days to deliver each litter was increased at the high dose for all litters;

the effect worsened progressively for the first four litters.

The last litter was reared by the parents until weaning. Although there were significantly fewer pups per litter at the high dose, the survival and growth of those pups to weaning was not affected by parental BBMP consumption. Animals from all dose groups and controls were kept and reared to test fertility of the second generation.

While the F_1 mice were growing, the control and high dose F_0 mice were cross-mated in Task 3. In this crossover mating trial, treated males were unaffected, but treated females were significantly affected: only one-third of the cohabited females delivered a litter; those litters had 30% fewer pups, who were approximately 8% lighter than their control counterparts. Thus, the effects seen during Task 2 were replicated by the treated females during Task 3.

After the Task 3 mating, the F_0 mice from the control and high dose groups were killed and necropsied. For the treated animals, female body weight was reduced by approximately 18%, and male body weight was reduced by approximately 12%. No organ weights were changed, nor were sperm end points or vaginal cyclicity affected.

In the Task 4 mating trial, all groups showed equivalent mating and fertility rates. Litters at the high dose were 33% smaller, and the pups weighed 13% less than their controls.

These F_1 adults were killed and necropsied. Female terminal body weights were reduced by 6% at the low dose and 18% at the high dose. Also at the high dose, relative liver weights were increased by 9%. For males, body weights at the middle and high doses were reduced by 9 and 25%, respectively. Absolute testis weight was reduced at the high dose by 16%, while relative liver weight was increased by 12%, and epididymal sperm density was reduced by approximately 14%. No changes were seen in estrous cyclicity.

This study found that 2,2-bis(Bromomethyl)-1,3-propanediol was both a general toxicant (reduced body weight gain and lower terminal body weights), as well as a female reproductive toxicant in the parental generation (fewer pups and lighter pups), and affected both sexes in the F_1 generation (pup effects, as well as reduced testis weight and epididymal sperm count). BBMP is not a selective reproductive toxicant, as these effects were seen concomitant with the general toxicity.

2, 2-BIS(BROMOMETHYL)-1,3-PROPANEDIOL

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB86168341/AS

Chemical: 2,2-bis(Bromomethyl)-1,3-propanediol

CAS#: 3296-90-0

Mode of exposure: Feed

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	0.1%	0.2%	0.4%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, ↓	↓, ↓
Kidney weight ^a		•	•	—, —
Liver weight ^a		•	•	—, —
Mortality		—, —	—, —	—, —
Feed consumption		—, —	—, —	—, —
Water consumption		•	•	•
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
\bar{x} litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	—, ↓	↓, ↓
Cumulative days to litter	—	—	↑
Absolute testis, epididymis weight ^a	•	•	—, —
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	0.4%	—

F ₁ generation	Dose concentration →	0.1%	0.2%	0.4%
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		—, —	—, —	—, —
Mortality		—, —	—, —	—, —
Adult body weight		—, ↓	↓, —	↓, ↓
Kidney weight ^a		—, —	—, —	—, —
Liver weight ^a		—, —	—, —	↑, ↑
Feed consumption		—, —	—, —	—, —
Water consumption		•	•	•
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	↓, ↓
Absolute testis, epididymis weight ^a	—, —	—, —	↓, —
Sex accessory gland weight ^a (prostate, seminal vesicle)	—, —	—, —	—, —
Epidid. sperm parameters (#, motility, morphology)	—, —, —	—, —, —	↓, —, —
Estrous cycle length	—	—	—

Summary information	
Affected sex?	Female
Study confounders:	None
NOAEL reproductive toxicity:	0.1%
NOAEL general toxicity:	<0.1%
F ₁ more sensitive than F ₀ ?	No
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.